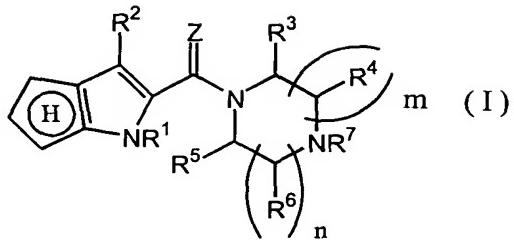
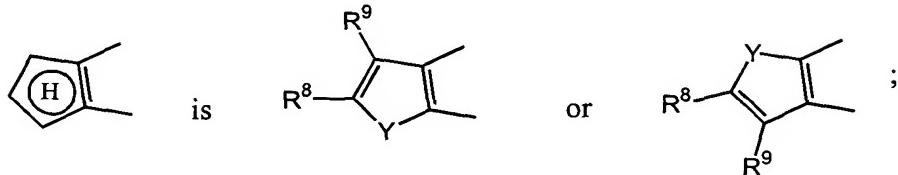


What is claimed is:

1. A compound of formula (I):



5 wherein



Y is O or S;

Z is O or S;

10 n is 1 or 2;

m is 1 or 2;

n + m is 2 or 3;

R¹ is H or C₁₋₆alkyl;

R² is H, F, Cl, Br or C₁₋₆alkyl;

15 R³ and R⁴ are, independently, H, C₁₋₄alkyl, C₃₋₆cycloalkyl,

C₁₋₄alkyl(C₃₋₆cycloalkyl), cyano, -CF₃, -(CO)NR^pR^q, -(CO)OR^r, -CH₂NR^pR^q

or -CH₂OR^r; where R^p, R^q and R^r are independently selected from H,

C₁₋₄alkyl, C₃₋₆cycloalkyl, phenyl, -C₁₋₂alkyl(C₃₋₆cycloalkyl), benzyl or phenethyl, or R^p and R^q taken together with the nitrogen to which they are

20 attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

25 R⁵ and R⁶ are, independently, H or C₁₋₆alkyl;

R⁷ is -R^a, -R^bR^a, -R^e-O-R^a or -R^e-N(R^c)(R^d), where R^a is H, cyano, -(C=O)N(R^c)(R^d), -C(=NH)(NH₂), C₁₋₁₀alkyl, C₂₋₈alkenyl, C₃₋₈cycloalkyl, C₄₋₇heterocyclic radical or phenyl, where the C₄₋₇heterocyclic radical is attached at a carbon atom and contains one of O, S, NH or NC₁₋₄alkyl, and optionally an additional NH or NC₁₋₆alkyl in rings of 5 or 6 or 7 members, where R^b is C₁₋₈alkylene or C₂₋₈alkenylene, where R^e is C₂₋₈alkylene or C₂₋₈alkenylene, where R^c and R^d are each independently H, C₁₋₄alkyl, C₂₋₄alkenyl, C₃₋₆cycloalkyl or phenyl, or R^c and R^d taken together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

alternatively, R⁷ may be taken together with an adjacent R⁴ as well as their carbon and nitrogen of attachment to form a 5, 6 or 7 membered heterocyclic ring, with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

R⁸ and R⁹ are, independently, H, F, Cl, Br, I, C₁₋₄alkyl, C₁₋₄alkoxy, -C₃₋₆cycloalkyl, -OC₃₋₆cycloalkyl, -OCH₂Ph, -CF₃, -OCF₃, -SCF₃, -(C=O)R^k (wherein R^k is H, C₁₋₄alkyl, -OH, phenyl, benzyl, phenethyl or C₁₋₆alkoxy), -(N-R^t)(C=O)R^k (where R^t is H or C₁₋₄alkyl), -(N-R^t)SO₂C₁₋₄alkyl, -(S=(O)_p)-C₁₋₄alkyl (wherein p is 0, 1 or 2), nitro, -SO₂NR^lR^m (wherein R^l and R^m are independently selected from H, C₁₋₄alkyl, phenyl, benzyl or phenethyl, or R^l and R^m taken together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₄alkyl), -(C=O)NR^lR^m, cyano or phenyl, where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

and enantiomers, diastereomers and pharmaceutically acceptable salts and esters thereof,

with the following provisos,

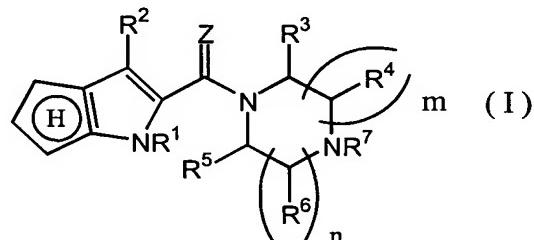
that R⁶ adjacent to N must be H where R⁴ adjacent to N is other than H,

5 that R⁷ is not -CH₂CH₂OH; and

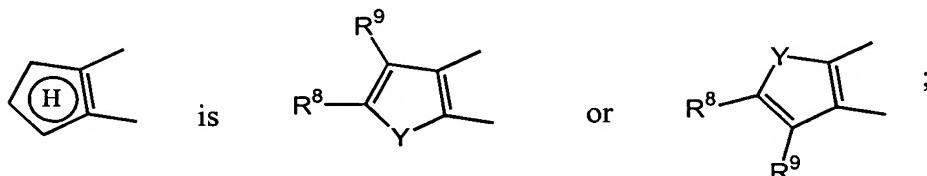
that where the core molecule is a 4H-furo, then one of R⁴ and R⁶ adjacent to N must not be methyl when the other is hydrogen unless R⁶ and R⁴ are taken together to form a bridging moiety.

2 A pharmaceutical composition containing a compound of formula (I):

10



wherein



15 Y is O or S;

Z is O or S;

n is 1 or 2;

m is 1 or 2;

n + m is 2 or 3;

20 R¹ is H or C₁₋₆alkyl;

R² is H, F, Cl, Br or C₁₋₆alkyl;

R³ and R⁴ are, independently, H, C₁₋₄alkyl, C₃₋₆cycloalkyl,

C₁₋₄alkyl(C₃₋₆cycloalkyl), cyano, -CF₃, -(CO)NR^pR^q, -(CO)OR^r, -CH₂NR^pR^q or -CH₂OR^r; where R^p, R^q and R^r are independently selected from H,

25 C₁₋₄alkyl, C₃₋₆cycloalkyl, phenyl, -C₁₋₂alkyl(C₃₋₆cycloalkyl), benzyl or phenethyl, or R^p and R^q taken together with the nitrogen to which they are

attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected

5 from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

R⁵ and R⁶ are, independently, H or C₁₋₆alkyl;

R⁷ is -R^a, -R^bR^a, -R^e-O-R^a or -R^e-N(R^c)(R^d), where R^a is H, cyano,

-(C=O)N(R^c)(R^d), -C(=NH)(NH₂), C₁₋₁₀alkyl, C₂₋₈alkenyl, C₃₋₈cycloalkyl,

10 C₄₋₇heterocyclic radical or phenyl, where the C₄₋₇heterocyclic radical is attached at a carbon atom and contains one of O, S, NH or NC₁₋₄alkyl, and optionally an additional NH or NC₁₋₆alkyl in rings of 5 or 6 or 7 members, where R^b is C₁₋₈alkylene or C₂₋₈alkenylene, where R^e is C₂₋₈alkylene or C₂₋₈alkenylene, where R^c and R^d are each independently H, C₁₋₄alkyl, C₂₋₄alkenyl, C₃₋₆cycloalkyl or phenyl, or R^c and R^d taken

15 together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

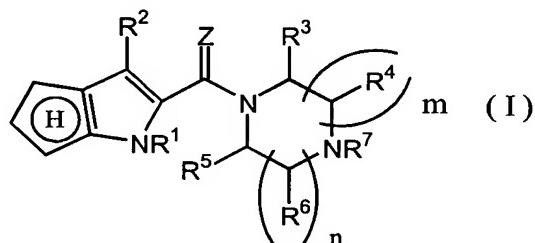
20 alternatively, R⁷ may be taken together with an adjacent R⁴ as well as their carbon and nitrogen of attachment to form a 5, 6 or 7 membered heterocyclic ring, with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and optionally and independently substituted with

25 between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;

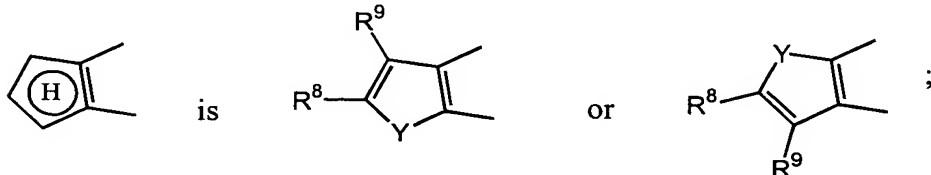
R⁸ and R⁹ are, independently, H, F, Cl, Br, I, C₁₋₄alkyl, C₁₋₄alkoxy, -C₃₋₆cycloalkyl, -OC₃₋₆cycloalkyl, -OCH₂Ph, -CF₃, -OCF₃, -SCF₃, -(C=O)R^k (wherein R^k is H, C₁₋₄alkyl, -OH, phenyl, benzyl, phenethyl or C₁₋₆alkoxy), -(N-R^t)(C=O)R^k (where R^t is H or C₁₋₄alkyl), -(N-R^t)SO₂C₁₋₄alkyl,

30 -(S=(O)_p)-C₁₋₄alkyl (wherein p is 0, 1 or 2), nitro, -SO₂NR^lR^m (wherein R^l and R^m are independently selected from H, C₁₋₄alkyl, phenyl, benzyl or phenethyl, or R^l and R^m taken together with the nitrogen to which they are

- attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₄alkyl), -(C=O)NR¹R^m, cyano or phenyl, where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy; and enantiomers, diastereomers and pharmaceutically acceptable salts and esters thereof,
- with the following provisos,
- that R⁶ adjacent to N must be H where R⁴ adjacent to N is other than H,
- that R⁷ is not -CH₂CH₂OH; and
- that where the core molecule is a 4H-furo, then one of R⁴ and R⁶ adjacent to N must not be methyl when the other is hydrogen unless R⁶ and R⁴ are taken together to form a bridging moiety.
- A method for the treatment or prevention of H₄-mediated diseases and conditions comprising the step of administering to a patient in need of such treatment or prevention a pharmaceutical composition containing an effective amount of a compound of formula (I):



wherein



- Y is O or S;
- Z is O or S;
- n is 1 or 2;
- m is 1 or 2;

n + m is 2 or 3;

R¹ is H or C₁₋₆alkyl;

R² is H, F, Cl, Br or C₁₋₆alkyl;

R³ and R⁴ are, independently, H, C₁₋₄alkyl, C₃₋₆cycloalkyl,

- 5 C₁₋₄alkyl(C₃₋₆cycloalkyl), cyano, -CF₃, -(CO)NR^pR^q, -(CO)OR^r, -CH₂NR^pR^q
or -CH₂OR^r; where R^p, R^q and R^r are independently selected from H,
C₁₋₄alkyl, C₃₋₆cycloalkyl, phenyl, -C₁₋₂alkyl(C₃₋₆cycloalkyl), benzyl or
phenethyl, or R^p and R^q taken together with the nitrogen to which they are
attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional
10 heteroatoms selected from O, S, NH or NC₁₋₆alkyl, and where any phenyl
or alkyl or cycloalkyl moiety of the foregoing is optionally and
independently substituted with between 1 and 3 substituents selected
from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;
- R⁵ and R⁶ are, independently, H or C₁₋₆alkyl;
- 15 R⁷ is -R^a, -R^bR^a, -R^e-O-R^a or -R^e-N(R^c)(R^d), where R^a is H, cyano,
-(C=O)N(R^c)(R^d), -C(=NH)(NH₂), C₁₋₁₀alkyl, C₂₋₈alkenyl, C₃₋₈cycloalkyl,
C₄₋₇heterocyclic radical or phenyl, where the C₄₋₇heterocyclic radical is
attached at a carbon atom and contains one of O, S, NH or NC₁₋₄alkyl,
and optionally an additional NH or NC₁₋₆alkyl in rings of 5 or 6 or 7
20 members, where R^b is C₁₋₈alkylene or C₂₋₈alkenylene, where R^e is
C₂₋₈alkylene or C₂₋₈alkenylene, where R^c and R^d are each independently
H, C₁₋₄alkyl, C₂₋₄alkenyl, C₃₋₆cycloalkyl or phenyl, or R^c and R^d taken
together with the nitrogen to which they are attached, form a 4-7
membered heterocyclic ring with 0 or 1 additional heteroatoms selected
25 from O, S, NH or NC₁₋₆alkyl, and where any phenyl or alkyl or cycloalkyl
moiety of the foregoing is optionally and independently substituted with
between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy,
amino, and C₁₋₃alkoxy;
alternatively, R⁷ may be taken together with an adjacent R⁴ as well as
30 their carbon and nitrogen of attachment to form a 5, 6 or 7 membered
heterocyclic ring, with 0 or 1 additional heteroatoms selected from O, S,
NH or NC₁₋₆alkyl, and optionally and independently substituted with

- between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;
- R⁸ and R⁹ are, independently, H, F, Cl, Br, I, C₁₋₄alkyl, C₁₋₄alkoxy, -C₃₋₆cycloalkyl, -OC₃₋₆cycloalkyl, -OCH₂Ph, -CF₃, -OCF₃, -SCF₃, -(C=O)R^k
- 5 (wherein R^k is H, C₁₋₄alkyl, -OH, phenyl, benzyl, phenethyl or C₁₋₆alkoxy), -(N-R^t)(C=O)R^k (where R^t is H or C₁₋₄alkyl), -(N-R^t)SO₂C₁₋₄alkyl, -(S=(O)_p)-C₁₋₄alkyl (wherein p is 0, 1 or 2), nitro, -SO₂NR^lR^m (wherein R^l and R^m are independently selected from H, C₁₋₄alkyl, phenyl, benzyl or phenethyl, or R^l and R^m taken together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, NH or NC₁₋₄alkyl), -(C=O)NR^lR^m, cyano or phenyl, where any phenyl or alkyl or cycloalkyl moiety of the foregoing is optionally and independently substituted with between 1 and 3 substituents selected from C₁₋₃alkyl, halo, hydroxy, amino, and C₁₋₃alkoxy;
- 10 15 and enantiomers, diastereomers and pharmaceutically acceptable salts and esters thereof,
- with the following provisos,
- that R⁶ adjacent to N must be H where R⁴ adjacent to N is other than H,
- that R⁷ is not -CH₂CH₂OH; and
- 20 that where the core molecule is a 4H-furo, then one of R⁴ and R⁶ adjacent to N must not be methyl when the other is hydrogen unless R⁶ and R⁴ are taken together to form a bridging moiety.